

**Local expansion in circulatory death kidney transplant activity improves wait-listed outcomes and addresses inequities of access to transplantation**

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**Local expansion in circulatory death kidney transplant activity improves wait-listed outcomes and addresses inequities of access to transplantation**

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Running title: **Wait-listed outcomes for DCD renal transplantation**

*Abbreviations:* CI, confidence interval; DBD, donation after brain-death; DCD, donation after circulatory death; eGFR, estimated glomerular filtration rate; ESRF, end-stage renal failure; FSGS, focal segmental glomerulosclerosis; IgA, immunoglobulin A; IQR, interquartile range; KDPI, kidney donor profile index; NHSBT, National Health Service Blood and Transplant; UK, United Kingdom

## Abstract

In the UK, circulatory death (DCD) kidney transplant activity has increased rapidly, but marked regional variation persists. We report how increased DCD kidney transplant activity influenced wait-listed outcomes for a single centre. Between 2002/03 and 2011/12, 430 (54%) DCD and 361 (46%) DBD kidney-only transplants were performed in the Cambridge Transplant Centre, with a higher proportion of DCD donors fulfilling expanded criteria status (41% DCD vs 32% DBD;  $P=0.01$ ). Compared to UK outcomes, where the proportion of DCD:DBD kidney transplants performed is lower (25%;  $P<0.0001$ ), listed patients at our centre waited less time for transplantation (645 vs 1045 days;  $P<0.0001$ ), with higher transplantation rates, and lower numbers of waiting-list deaths. This was most apparent for elderly (>65 years) patients (waiting time 730 vs 1357 days nationally;  $P<0.001$ ), who received predominantly DCD kidneys from old donors (mean donor age 64), whereas younger recipients received equal proportions of living-donor, DBD and DCD kidney transplants. Death-censored kidney graft survival was nevertheless comparable for young and elderly recipients, although transplantation conferred a survival benefit from listing for only younger recipients. Local expansion in DCD kidney transplant activity therefore improves survival outcomes for younger patients and addresses inequity of access to transplantation for elderly recipients.

Introduction

The number of kidney transplants from donation after circulatory death (DCD) donors has risen rapidly in the UK over the last ten years (1). From a baseline of approximately 100 transplants per annum prior to 2003/04, over 800 DCD kidney transplants were performed in 2013/14, with DCD transplantation now representing approximately 40% of all deceased-donor renal transplant activity in the UK. Worldwide, only the Netherlands achieves similar DCD donor rates per million population (1).

Several aspects of this expansion merit consideration. Firstly, it has been accomplished through acceptance of increasingly elderly donors: in 2003/04 the mean age of DCD kidney donors nationally was 43, whereas in 2013/14 this was 54; significantly greater than the contemporaneous donation after brain death (DBD) cohort (mean age 49,  $P<0.0001$ ). Consequently, almost half the DCD kidneys currently transplanted in the UK fulfil criteria for expanded donors (ECD) on the basis of donor age greater than 60. Secondly, the expansion in DCD kidney transplantation in the UK has not occurred uniformly, and marked regional differences persist in DCD donation rates (2). This is important, because unlike DBD kidneys, DCD kidneys were, until September 2014 (3), not allocated nationally; instead both kidneys were offered to the local renal transplant centre. Consequently, DCD kidney transplant activity in the different UK renal transplant centres varies widely; representing less than 10% of deceased donor transplant activity in some centres and greater than 60% in others (4).

Following the introduction of a programme to expand DCD kidney transplantation (5-7), the Cambridge Transplant Centre now performs approximately twice as many DCD as DBD kidney transplants. Studies to date have generally focused on comparing outcomes of DCD and DBD kidneys *from transplantation* (5-14). However, given the difference in allocation

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3 policy for DCD and DBD kidneys, in which utilisation of a local DCD resource will impact  
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5 upon access to the national DBD pool, we sought to examine how an alteration in the  
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7 balance of deceased kidney transplants impacted on outcomes *from listing*, with particular  
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9 consideration whether any distinct waiting list cohort has been more or less advantaged.  
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11 Because variation in patterns of DCD kidney transplantation across UK transplant centres  
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13 persists, this further enabled the analysis of outcomes from listing for Cambridge patients to  
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15 be compared to those achieved in units in which DCD kidney transplant activity had not  
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17 increased as dramatically. In the absence of a prospective trial, such comparison provides a  
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19 means of validating that observed differences were related to different DCD kidney  
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21 transplant practices.  
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**Materials and Methods**

***Study population and design***

The study population comprised all adult patients ( $\geq 16$  years,  $n=1459$ ) listed for deceased renal transplantation at our centre from 1<sup>st</sup> August 2002 to 31<sup>st</sup> July 2012. Recipients were categorised according to age at listing:  $<45$  years old; 45 to 65 years old; and  $\geq 65$ -years-old, with the following exclusion criteria: multiple organ transplantation ( $n=36$ ); transfer to our centre whilst on the waiting list ( $n=10$ ); transfer away from our centre whilst on the waiting list ( $n=22$ ); and travel overseas for transplantation ( $n=10$ ). During this period, a further eight patients received living donor kidney transplants but were never listed for deceased donor transplantation and were therefore not included in the analysis. National data (with data for the Cambridge Transplant Centre omitted) was obtained from the UK transplant registry database held by NHS Blood and Transplant (NHSBT) only, whereas data for the Cambridge Transplant Centre was amalgamated from case notes, a prospectively maintained local database, and the NHSBT database.

Study end-points were defined as patient death, cease of engagement with local centre (including transferring out of area), or formal study completion (31<sup>st</sup> July 2012), with the primary outcome the fate of listed patients: progression to transplantation; removal from waiting list without transplantation; suspension from waiting list (generally due to illness from which recovery is anticipated); remaining actively listed; and death. Patients listed or transplanted from 2009 onwards were assumed to have correct follow-up entered on the local and NHSBT databases; cases prior to 2009 were reviewed individually to identify follow-up dates. All-cause graft survival was defined as the time of transplant to time of return to renal replacement therapy or death. Patient survival was defined as time from listing to death. For the purposes of outcome from listing, patients re-listed after a

previously failed transplant, even if previously included, were considered as a new listing (n=207). In order to demonstrate how deceased donors used in Cambridge compared with those used elsewhere in the UK, data was obtained from NHSBT for all deceased donors transplanted into adult recipients (age over 18) in Cambridge and the rest of the UK between 2002 and 2012. Donor age, type (DCD vs DBD) and criteria (standard vs expanded) were analysed according to financial year (1<sup>st</sup> April to 31<sup>st</sup> March).

All DCD kidneys were procured from controlled, Maastricht category 3/4 (15) donors who incurred irrecoverable brain injury, but did not meet the criteria for diagnosis of brainstem death. DCD organ procurement for our centre has been detailed previously (5-7, 16, 17), and differs from standard US practice in that organ donation was pursued for a minimum of four hours after withdrawal of life-supporting treatment, irrespective of the agonal phase characteristics (6). Expanded criteria donors (ECD) were defined as those  $\geq 60$  years or those aged 50-59 years with two of the following three features: hypertension; terminal serum creatinine  $>132$  mmol/L; or death from cerebrovascular accident (18). Donors with acute kidney injury (high terminal creatinine) were considered for kidney donation only when recent tests indicated satisfactory baseline renal function; 49 patients received kidneys from donors with terminal creatinine  $>200$  mmol/L (range 200 – 504 mmol/L).

### ***Organ allocation***

Kidneys from DBD donors were allocated according to the national algorithm as outlined by NHSBT (the Deceased Donor Kidney Allocation Scheme (3)): firstly, paediatric patients were favoured over adult patients; then 000 HLA-mismatched kidneys were prioritised (with preference to highly-sensitised or HLA-homozygous individuals). Beyond this, allocation was based on a points system, according to an algorithm incorporating: waiting time; HLA match; age; age difference; geographical location; blood group; and HLA type. Although the

allocation algorithm was altered in 2006, the same algorithm applied to all patients on the waiting list at any one time and there was no difference in the age-related components of the algorithms. During the study period, DCD kidneys were not allocated nationally, but DCD kidneys were offered on a regional basis (20 regions in the UK) to the local transplant centre that covered that region. The centres were at liberty to select recipients felt most suitable for these kidneys, and no formal arrangement existed for sharing with other regional centres. At the Cambridge Transplant Centre, a similar algorithm to that used nationally for DBD kidneys was used to select recipients for DCD kidneys, but with the ability to limit the algorithm to select only elderly recipients (typically over 60 years old) for kidneys deemed more 'marginal' at the discretion of the on-call team. As described previously (5, 7), pre-implantation biopsy analysis was used routinely to help determine the suitability of elderly deceased-donor kidneys for transplantation. Living donor transplants were arranged according to standard UK practice.

**Data and statistical analysis**

Data obtained for each patient included: date of birth, sex, date of end-stage renal failure (ESRF) diagnosis, date of pre-emptive listing, date of graft failure if previously transplanted, cause of ESRF, previous transplantation, date of listing, date of transplantation, date of death, cause of death, date of removal from list, date of suspension from list, date of graft loss, cause of graft loss, donor age, donor type (whether DBD, DCD, or living). Graft and patient survival were calculated using Kaplan-Meier estimates and log-rank tests for statistical significance. In the comparison of patient survival from listing (Figure 6c), only survival from the time of listing for the first transplant was analysed. For the elderly cohort, comparison of survival for those transplanted against those remaining on the waiting list was also assessed by the time-dependent non-proportional Cox regression model (19),



adjusting for primary disease, ethnicity, gender, blood group, BMI, and sensitisation status.

Median waiting times for deceased donor-kidney transplantation were calculated using Kaplan-Meier method of estimation, by excluding patients that were transplanted using a kidney from a living donor, and censoring for removals (ill-health or recovery of renal function) or deaths on the list. Rates of de-listing for transplantation (death or removal from the list without transplantation) were also estimated by Kaplan-Meier analysis, by censoring for transplantation. The Kidney Donor Profile Index (KDPI) was calculated using the 2014 reference dataset (20). Categorical data were examined with the Chi-squared test, non-parametric continuous data were assessed using Kruskal-Wallis test and parametric continuous data with Student's *t* test. Statistical analysis was performed using SAS (v9.1; SAS Institute, Cary NC, USA), and GraphPad Prism (v 5.03; GraphPad Software Inc, CA, US.).

Results

Changing profile of deceased kidney transplants

A single-centre, retrospective observational cohort study was performed to examine outcomes for all adult patients listed for kidney transplantation at the Cambridge Transplant Centre between 2002/03 and 2011/12. As reference, during this period the number of DCD adult kidney only transplants performed increased markedly; from 11 in the 2002/03 financial year to 68 in the 2011/12 financial year (Figure 1A), which represents a much higher proportion of deceased donor kidney transplantation than occurred nationally (Figure 1B). Figure 1A also shows that numbers of living donor kidney transplants increased over the study period, but to a lesser extent, whilst numbers of DBD kidney transplants remained relatively static. In keeping with national trends, the age of the DCD kidney donors increased throughout the study period (Figure 1C. Consequently, compared to the DBD kidney transplants, a significantly higher proportion of the DCD kidney transplants performed were from ECD donors (DBD; 33% (114 of 346) vs. DCD; 44% (186 of 426),  $\chi^2$   $P=0.003$ ).

Elderly listed patients are less likely to receive a kidney transplant

To assess how the expansion in availability of predominantly elderly DCD kidneys impacted upon the recipient pool, outcomes from listing for study patients were compared according to three listed-patient groups: younger than 45 years old; from 45 to 65 years old; and older than 65 years at listing for kidney transplantation (Table 1). Transplant outcomes and donor details are listed in Table 2. Over the entire study period, elderly listed patients were less likely to be transplanted, and more likely to be removed from the waiting list, than younger patients (Table 2). Nevertheless, comparison of outcomes from listing at 1, 3 and 5 years

with national data (Figure 2) demonstrated that for all age groups, patients on the Cambridge waiting list were more likely to be transplanted than their equivalent UK cohort. This difference was more marked for the elderly: whereas 59% of Cambridge-listed patients over 65 years old were transplanted by five years, only 38% of the equivalent national waiting-pool had received a kidney transplant ( $P<0.001$ ; Chi-Squared test). Conversely, a greater proportion of elderly listed patients nationally were either removed from the list or died before transplantation (at five years: Cambridge 41% vs National 46%;  $P<0.001$ ).

### ***Higher rates of delisting for elderly waiting list patients***

Comparison of the rate of removal of patients from the waiting-list due to death or ill-health was further assessed by Kaplan-Meier analysis of outcomes for the Cambridge listed patients (Figure 3). This confirms that rates of delisting were significantly higher for the cohort of elderly listed patients, with less than 50% of patients over 65 years old who were listed, but not transplanted, still active on the list after four years. Analysis of the UK dataset also revealed that the rate of removal from the waiting list was significantly higher for the elderly cohort, but that for each age range, delisting rates were similar to those observed in Cambridge (Figure 3), suggesting that the smaller proportion of elderly patients dying or being removed from the waiting list in the Cambridge Transplant Centre does not reflect a bias to listing relatively fitter recipients.

### ***Donor profiles differ markedly according to recipient age***

In considering why elderly listed patients in Cambridge have greater access to transplantation, analysis of the type of kidneys transplanted into each recipient age group reveals marked differences (Table 2). Whereas the proportions of living-donor, DCD and DBD kidney transplants were broadly equivalent for listed recipients under 45 years old,

patients over 65 received kidney transplants from predominantly DCD donors, with DBD and living donors together constituting only approximately one-third of the transplants performed. Numerically, most DCD kidneys were nevertheless transplanted into recipients in the younger age groups (Table 2).

In keeping with the older age of DCD kidney donors, elderly patients generally received kidney transplants from more elderly donors (Figure 4, Table 2). Calculation of the KDPI donor score revealed that these kidneys could be considered extremely marginal (Table 2), with 69% of kidneys transplanted into the elderly cohort scoring greater than 85.

The relatively rapid rate of removal of elderly patients from the waiting list due to death or illness suggests that local availability of DCD kidneys may be a particularly important factor underlying the difference in Cambridge and National transplantation rates for elderly recipients. In support, comparison of Cambridge and National waiting times for kidney transplantation (Figure 5) highlights that waiting times for the three recipient age groups were comparable for Cambridge patients, but that elderly patients waited substantially longer nationally. Moreover, waiting times for our elderly patients fell during the study period (Figure 5); presumably reflecting the continued expansion of the DCD kidney transplant program. Although the simultaneous increase in living donor transplant activity in our centre (Figure 1a) would be expected to contribute to a fall in waiting times, the impact is likely to be less pronounced than for the DCD kidney transplant program, because substantially fewer living donor kidney transplants were performed at our centre during the study period than DCD kidney transplants (283 vs 426; including 8 living donor recipients never listed for a deceased donor transplant (Figure 1a)). It should also be noted that, compared to the UK, our living donor program has remained relatively small during the

study period (283 of 1088 (26%) kidney transplants performed in Cambridge vs. 7976 of 22163 (36%;  $P < 0.0001$ ) performed nationally). Similarly, the fall in the Cambridge waiting times was most apparent for the 45-65 and  $>65$  recipient age groups (Figure 5) and in both cohorts, DCD transplant activity was dominant (Table 2).

The reason that elderly UK patients are apparently disadvantaged in their access to DBD kidney transplantation is not immediately obvious, but we thought it likely a facet of the algorithm for national sharing of DBD kidneys (21), whereby younger recipients of DBD kidneys generally score more highly than elderly. Consequently, elderly recipients must wait longer to accrue sufficient waiting-time points on the algorithm to outcompete younger recipients (Figure 5 and Table 3). Although DCD kidneys were not allocated nationally during the study period, application of the algorithm to our recipients revealed that for all age groups, the allocation score was less for Cambridge DCD recipients than for nationally allocated DBD kidneys (Table 3). This is partly due to the smaller local recipient pool that generally prevents close HLA-matching between donor and recipient, but mostly reflects the much shorter waiting times for transplantation.

#### ***Kidney transplant outcome and patient survival from listing***

Outcomes for DCD kidney transplantation in our unit have been described previously (5-7) and report similar outcomes for DCD and DBD kidney transplantation. All-cause kidney graft survival was poorer for elderly recipients (Figure 6a), but largely reflects that 12 of 18 graft losses in this group were due to recipient death (generally due to malignancy or sepsis) with a functioning graft (median pre-terminal creatinine  $151 \mu\text{mol/l}$ ). Graft survival when censored for recipient death was comparable for the three recipient groups (Figure 6b). In anticipation that the impact of increased kidney transplant activity would be most apparent

in an assessment of recipient outcomes that included time on the waiting list, recipient survival for each age group was assessed from the point of listing and compared to those listed patients who did not receive a transplant (Figure 6c). This analysis confirms that transplantation was associated with improved survival for patients in the two younger age groups, but not for the elderly cohort. An additional non-proportional Cox regression model analysis (19) was performed to compare survival for the elderly cohort who received a transplant against those who remained on the waiting list. This also failed to show a survival advantage for transplantation in the elderly (Hazard ratio = 1.87 (95% CI 0.42-8.26);  $P = 0.4$ ).

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## Discussion

The rate of expansion of DCD kidney transplantation in the UK has been remarkable. However marked variations in regional Intensive Care Unit DCD donation rates (2), allied to apparent differences between transplant centres in the assessment of suitability of DCD kidneys for transplantation, has resulted in geographical fragmentation of current DCD kidney transplant activity. The major consequence of this piecemeal implementation is that transplanting increasing numbers of locally-resourced DCD kidneys will, for a particular centre, likely restrict access of that centre's listed population to the nationally-allocated DBD kidney pool; one of the major factors determining national allocation is waiting-time for a transplant. The impact of this apparent conflict between local DCD kidney and national DBD kidney allocation would be potentially more marked if, as was once generally considered, DCD kidneys were of inherently poorer quality than DBD kidneys, but analyses of individual centre (5, 7) and National UK transplant data (8, 9) have demonstrated that age-matched outcomes for DCD and DBD kidney transplantation are similar. Nevertheless, increased use of a local circulatory death donor pool would potentially result in transplantation of less well-matched kidneys from older donors than the recipients would have otherwise received from the national DBD pool. Hence we felt it important to analyse how the marked expansion in DCD kidney transplantation in our centre has affected recipient outcomes, but to focus this analysis on outcomes from listing for various age groups of the waiting list population. Our analysis suggests waiting times for transplantation are improved for all recipients, and given the equivalent outcomes from transplantation for DCD and DBD kidneys in our centre (5-7), that this is associated with improved survival outcomes from listing in recipients under 65 years old. The situation is more complex for

older recipients, because although this group arguably gains most in terms of equity of access to transplantation, their survival is not enhanced by transplantation.

There are potentially several reasons why elderly listed patients are generally disadvantaged in their access to transplantation. Our analysis highlights that options for living-donor transplantation for our elderly recipients are generally more limited than for younger recipients, presumably either because of concerns relating to fitness of the spouse or because living donation from offspring to parent is not perceived as acceptable as parent to offspring donation. The apparent inequity of access of elderly recipients to the national DBD pool is largely due to the UK matching algorithm for DBD kidney allocation (21). The algorithm calculates an allocation score for level 1, 2 and 3 HLA-mismatched kidneys based on, among other factors: waiting-time for transplantation; the degree of HLA matching; and age difference between donor and recipient, but was designed specifically ‘to ensure well-matched transplants for younger patients while recognizing that HLA matching is less important for older patients’. Thus the algorithm is weighted to preferentially allocate more closely HLA-matched kidneys to younger recipients, irrespective of donor/recipient age difference. Accordingly, younger recipients receive an exponentially greater number of points than elderly recipients for receipt of a well-matched kidney, and a crude analysis of the algorithm suggests that the elderly cohort would need to accrue approximately four years’ waiting-time points to compensate for this bias to younger recipients. This carries the major drawback that, as highlighted by our analysis, the window for transplantation of elderly listed recipients is small and that approximately half of these patients will either have died or become too frail to transplant by four years. This presumably explains why, when compared to younger listed recipients, only approximately half as many elderly listed



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3 patients nationally receive a transplant, and yet at five years the percentage of patients still  
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5 waiting for transplantation is similar for both groups (~15%, see Figure 2).  
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8 We ostensibly adopted the same algorithm as used nationally for allocating local DCD  
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10 kidneys to our recipients, and it is perhaps surprising that this enabled us to transplant our  
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12 elderly recipients. Our elderly recipients generally received kidneys from elderly DCD donors  
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14 (Table 2) and we think this is partly a consequence of a relative reduction, when compared  
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16 to the national DBD pool, in the size of the local DCD donor pool that limits availability of  
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18 well-matched younger recipients for a proportion of the elderly DCD donors. However, local  
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20 allocation of DCD kidneys provided the flexibility to impose additional restrictions on  
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22 recipient selection. We have also, at the clinicians' discretion, deliberately chosen to  
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24 allocate kidneys from elderly DCD donors that were deemed more 'marginal' to only elderly  
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26 recipients, and it is notable that a substantially higher proportion of the DCD than DBD  
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28 kidneys transplanted fulfilled ECD status. This mirrors the strategy adopted by the  
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30 Eurotransplant Senior Program (22), in which kidneys from elderly donors are preferentially  
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32 transplanted into elderly recipients. Our analysis provides further support for the benefits of  
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34 this approach. The kidneys transplanted into our elderly recipients (mainly from elderly DCD  
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36 donors) could be considered extremely marginal, with 69% having a KDPI score greater than  
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38 85, and yet graft outcomes were generally favourable and prejudiced mainly by recipient  
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40 death with a functioning graft. The surprisingly good outcomes for these kidneys may reflect  
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42 our routine use of pre-implantation biopsy analysis to help determine suitability for  
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44 transplantation (5, 7).  
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53 Irrespective, it is clear that the availability of locally-allocated DCD kidneys has enabled us to  
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55 transplant a far greater proportion of our transplant waiting list than would otherwise be  
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the case. The short waiting time for transplantation achieved, currently the lowest in the UK (23), has substantially improved the opportunity for transplanting our elderly listed recipients. As the haemodialysis population ages (24), it is likely that greater numbers of elderly patients will continue to be listed for kidney transplantation; their deliberate selection as recipients of elderly DCD kidneys may provide an opportunity for transplantation not otherwise afforded. In this regard, our findings are likely to have relevance beyond UK transplant practice. Death on the waiting list appears to be an even greater problem for elderly patients in the United States (25), and yet the recent introduction of the US Kidney Allocation System has been associated with increased discard rates of kidneys with highest KDPI scores (26), and has seen a fall in transplant rates for elderly listed patients and an increase in their waiting time for transplant (27). Given that kidneys with high KDPI are typically from ECD circulatory death donors, and that such kidneys are allocated locally rather than nationally, our findings suggest that their preferential allocation to elderly listed patients may provide an opportunity for transplantation for these recipients not otherwise available.

One concern raised by our analysis is whether it is appropriate, in the absence of a demonstrable survival benefit for transplantation, to continue to allocate organs to elderly recipients that may otherwise improve survival of younger recipients. The apparent lack of survival benefit for transplantation in our elderly cohort is surprising, because previous analyses from the UK have suggested otherwise (28, 29), but does not appear to relate to the limited number of elderly patients in our study; in contrast to the younger cohorts, the survival curves for the elderly transplanted and the elderly that remained on dialysis are closely matched (Figure 6C). This may relate to continuing improvements in survival for elderly patients with end-stage renal failure on haemodialysis (24). Nevertheless, we feel it

justifiable to continue to list elderly recipients on the basis of patient choice and improvement in quality of life (30, 31). In addition, even allowing for deliberate selection of elderly recipients for kidneys deemed more marginal, proportionally fewer of the elderly than younger listed patients ultimately received a kidney transplant (Table 2), and it is therefore difficult to argue that the elderly have been unfairly advantaged by our selection policy. Moreover, those patients over 65 years old listed during the study period represent less than 10% of all listed patients, and it should be stressed that the majority (89%) of DCD kidneys in our study were transplanted into patients under 65 years old at time of listing. Hence, although the Cambridge DCD program appears to perhaps have made the biggest difference to outcomes for elderly listed patients, the greatest impact has instead been on younger listed patients, with the many more transplants realised by the program conferring improved survival from listing.

In summary, our analysis demonstrates that local expansion in DCD transplant activity can improve outcomes for young and elderly listed patients. For elderly listed recipients, an awareness that their window for transplantation is likely to be narrow may justify increased use of 'marginal' kidneys with high KDPI scores.

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**Disclaimer**

The views expressed in this manuscript are those of the authors and not necessarily those of the NHS, the NIHR, the Department of Health or NHSBT National Institute of Health Research Blood and Transplant Research Unit.

**Disclosure**

The authors of this manuscript have no conflicts of interest to disclose as described by the American Journal of Transplantation.

## Figure Legends

### Figure 1: Changing profiles of deceased kidney donors

(A) Numbers of expanded criteria donor (ECD) and standard criteria donor (SCD) kidneys transplanted at the Cambridge Transplant Centre according to deceased donor type (donation after brain death (DBD) and donation after circulatory death (DCD)). Numbers of living donor transplants (LD) are included for comparison. (B) DCD kidney transplants, as a percentage of deceased donor kidney transplants in Cambridge and the UK (C) Regression lines of donor age superimposed on graphs depicting median and interquartile range of donor age per year for Cambridge DBD and DCD donors:  $P=0.047$ , analysis of covariance. Year denotes financial year.

### Figure 2: Comparison of outcomes for wait-listed patients nationally and at the Cambridge Transplant Centre

Waiting list status at one, three and five years from listing of patients listed for renal transplantation between 2002 and 2008 nationally and locally (at the Cambridge Transplant Centre) according to age at listing:  $n=7118, 8620, 1837$  for national and  $375, 459$  and  $59$  for local patients listed aged under 45, 45 to 65, and over 65 years, respectively.  $*P<0.05$ ;

$**P<0.001$ ; Fisher's Exact Test.

**Figure 3: Rates of delisting from kidney transplant waiting list**

Kaplan-Meier analysis of rates of delisting (due to death or removal from the waiting list and censored for transplantation) for patients listed at the Cambridge Transplant Centre (dotted line) and in the rest of the UK (solid line), according to age at listing for transplantation. Log-rank analysis confirms that at the Cambridge Transplant Centre, elderly (>65 years) patients were delisted significantly more rapidly than younger patients ( $P < 0.01$ ), but that for any age cohort, local (Cambridge) rates of delisting were not different from UK rates ( $P = \text{NS}$ ).

**Figure 4: Differences in donor profiles according to recipient age at listing**

Scatterplot depicting deceased donor age for each recipient group (Kruskal-Wallis  $P < 0.0001$ ).

**Figure 5. National and Cambridge waiting times according to recipient age**

Waiting time to adult kidney transplantation in the UK and Cambridge according to age at listing and year of listing. Graph shows median +/- confidence intervals and  $P$  values depict log-rank analysis.

**Figure 6. Kidney graft and patient survival.**

Kaplan-Meier curves and numbers at risk for (A) all-cause graft survival ( $P=0.0004$ ; Log-Rank test) and (B) graft survival censored for death as a cause of graft loss according to age at listing ( $P=0.2705$ ). (C) Kaplan-Meier curves and numbers at risk for patient survival from first listing in transplanted (black line) and non-transplanted patients (grey line) for those aged: under 45 (left); 45 to 65 (middle); and over 65 (right); at time of listing.

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Table 1

	Age at listing			P-value
	Under 45	45 to 65	Over 65	
Number of patients listed	557	688	136	
Age at listing (Median, range)	36.2 (16.2-45.0)	55.0 (45.0-65.0)	67.9 (65.1-75.5)	
Median length of follow-up in days* (range)	1519 (0-3624)	1271 (0-3648)	1164 (26-3592)	
Sex <sup>+</sup>				P=0.47
Male	343 (62%)	445 (65%)	89 (65%)	
Female	214 (38%)	243 (35%)	47 (35%)	
Cause of ESRF <sup>+</sup>				P<0.0001
Cystic kidney disease	64 (11.5%)	<b>162 (23.6%)</b>	<b>15 (11.0%)</b>	
Diabetes mellitus	38 (6.8%)	<b>73 (10.6%)</b>	11 (8.1%)	
Glomerulonephritis	42 (7.5%)	66 (9.6%)	<b>14 (10.3%)</b>	
IgA nephropathy	<b>68 (12.2%)</b>	53 (7.7%)	11 (8.1%)	
Pyelointerstitial Nephritis	<b>90 (16.2%)</b>	40 (5.8%)	8 (5.9%)	
Systemic	27 (4.9%)	47 (6.8%)	10 (7.4%)	
Other	<b>228 (40.9%)</b>	<b>247 (35.9%)</b>	<b>67 (49.3%)</b>	
Pre-emptively listed <sup>+</sup>	83 (15%)	53 (7.7%) (1 unknown)	5 (3.7%)	P<0.0001
Previous transplant <sup>+</sup>	117 (21%)	85 (12%)	5 (3.7%)	P<0.0001

Table 2

	Age at listing			P value
	Under 45	45 to 65	Over 65	
Number listed	557	688	136	
Outcomes <sup>+</sup>				$P < 0.0001$ <sup>†</sup>
Transplanted	411 (73.8%)	479 (69.6%)	72 (52.9%)	
Suspended	42 (7.5%)	115 (16.7%)	9 (6.6%)	
Removed or died	20 (3.6%)	14 (2.0%)	30 (22.1%)	
Remained active	84 (15.1%)	80 (11.6%)	25 (18.4%)	
Age at transplantation (Median, range)	37 (17-49)	57 (45-70)	69 (66-75)	
Donor age <sup>**</sup> (Median, range)	44 (1-70)	56 (2-82)	67 (23-79)	$P < 0.0001$ <sup>xx</sup>
Donor type (%) <sup>+</sup>				$P < 0.0001$ <sup>†</sup>
DBD	127 (31%)	119 (25%)	17 (24%)	
DCD	130 (32%)	243 (51%)	45 (63%)	
Live donor	154 (37%)	117 (24%)	10 (14%)	
*KDPI <sup>**</sup> (Median, range)	46 (1-100)	77 (1-100)	94 (18-100)	$P < 0.0001$ <sup>xx</sup>
Graft failure (% of transplanted)				
All cause	49 (11.9%)	60 (12.5%)	18 (25%)	
Censored for death	42 (10.2%)	45 (9.4%)	6 (8.3%)	
Death (% of listed)	40 (7.2%)	59 (8.6%)	26 (19%)	
With transplant	13 (2.3%)	20 (2.9%)	15 (11%)	
Without transplant	27 (4.8%)	39 (5.7%)	11 (8.1%)	

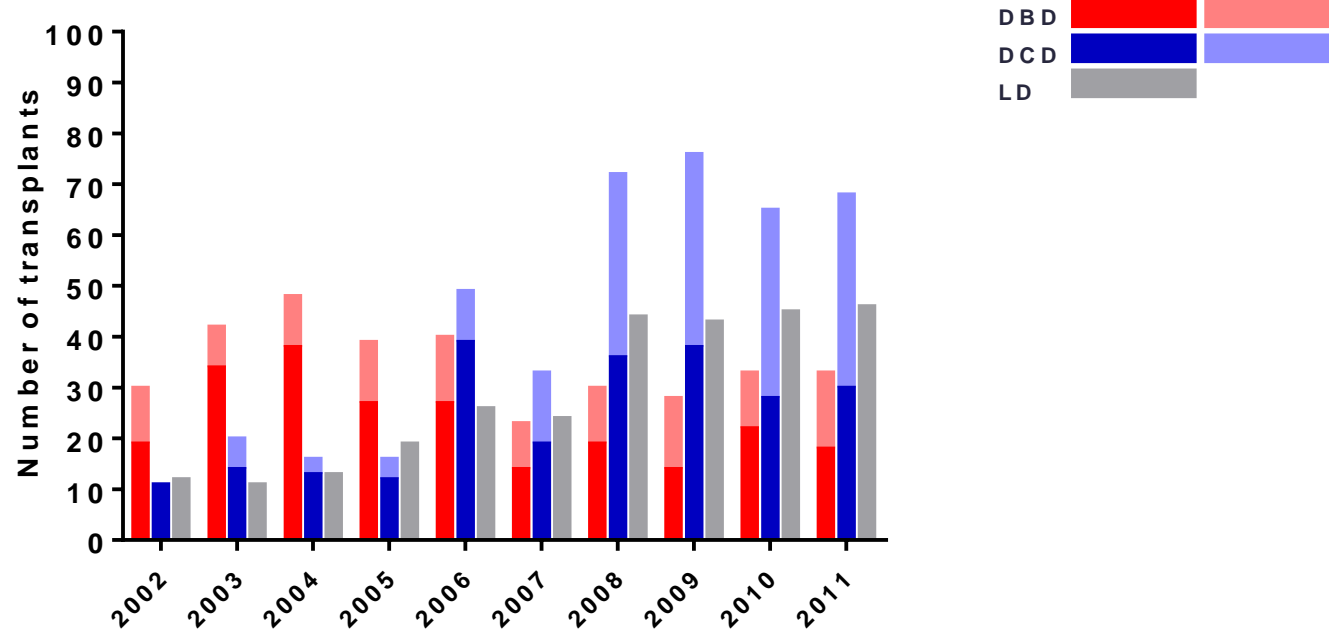
Table 3

Age at listing	National DBD Kidney Transplants		Local DCD Kidney Transplants		<i>P</i> -value
	Number of transplants	Median KAS (IQ Range)	Number of transplants	Median KAS (IQ Range)	
Under 45	2593	3201 (2709 – 3757)	107	2178 (1563 – 2609)	<0.0001
45 to 65	3274	2771 (2156 – 3332)	200	1582 (1300.3 – 2002)	<0.0001
Over 65	654	2327 (1622 – 2909)	33	1385 (1044.5 – 1603)	<0.0001

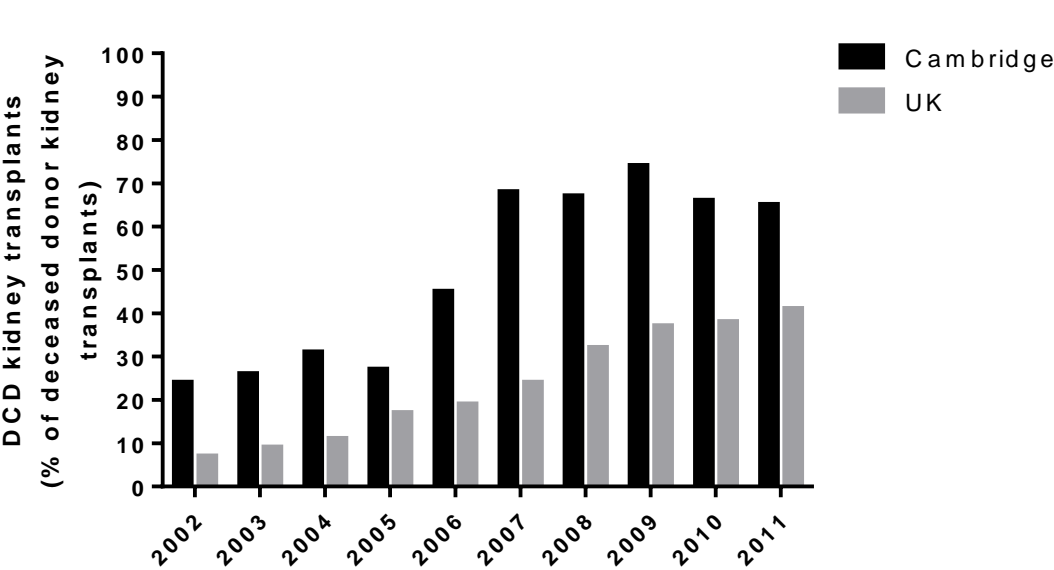
CONFIDENTIAL

Figure 1

A



B



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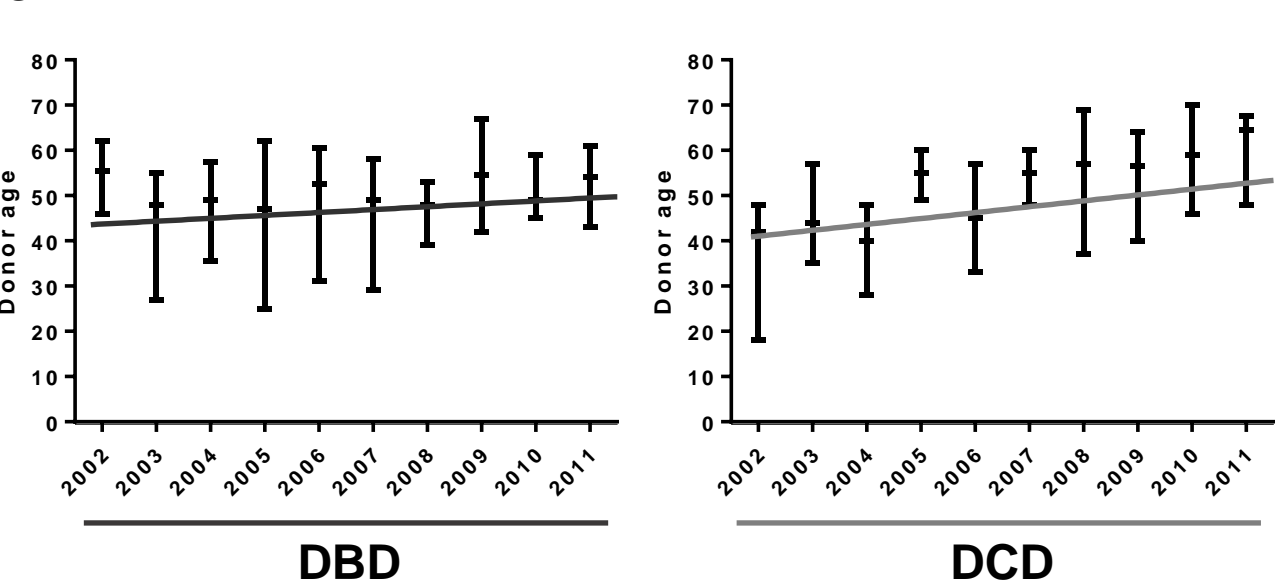


Figure 2

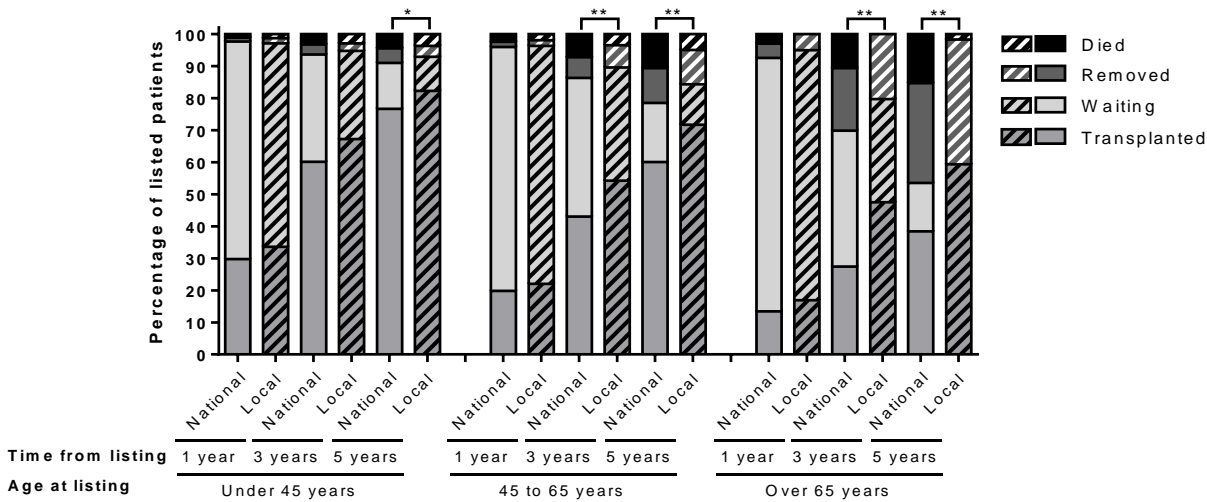
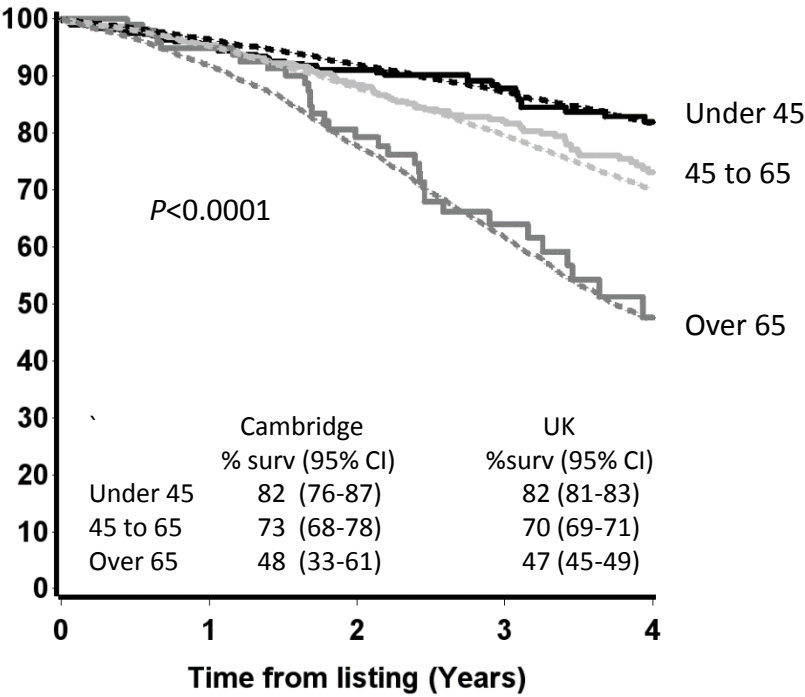




Figure 3



Under 45	UK	10017	6975	5043	3192	1958
	Cambridge	559	330	221	134	77
45 to 65	UK	13343	10634	8262	5625	3464
	Cambridge	731	497	319	202	119
Over 65	UK	3031	2470	1860	1187	675
	Cambridge	117	84	54	27	12

Numbers at risk

Figure 4

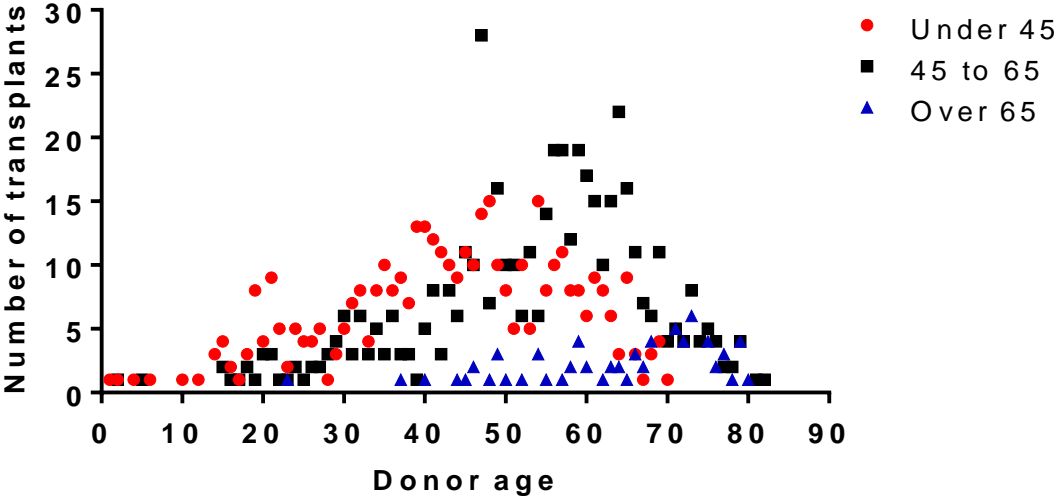


Figure 5

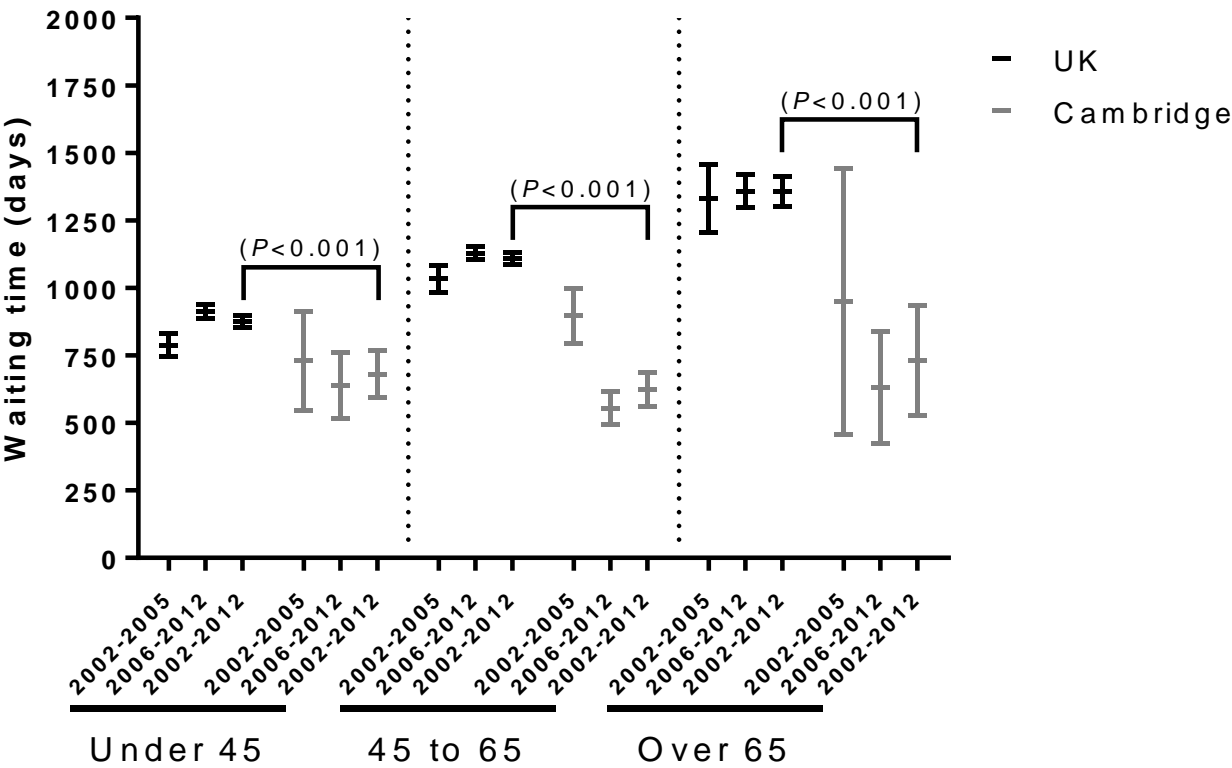


Figure 6

